

## The Epigenetic Clock and Longevity

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**Received:** December 10, 2016; **Published:** December 14, 2016

Many alterations occur to our genome or DNA as we age. Some of these changes are epigenetic modifications to our DNA without altering the genetic sequence itself. The human genome is the complete assembly of DNA (deoxyribonucleic acid) that makes each individual unique. The genome consists of about 3 billion base pairs...half from the mother and half from the father. DNA holds the instructions for building the proteins that carry out a variety of functions in a cell. Chemical compounds and proteins that can attach to DNA comprise what is known as the epigenome. These epigenomic compounds attach to DNA as “tags” and change the way individual cells use the DNA’s instructions. Importantly these tags or “marks”... as they are known... do not change the sequence of the DNA but rather how the cells operate.

It is known that the age of many human tissues and cells is reflected by chemical changes to DNA. These changes affect how cells in different parts of the body use the same genetic code. One such modification, known as methylation, occurs when methyl group “tags” attach to DNA in specific places. These methyl groups turn genes on or off by affecting interactions between the DNA and other proteins. The result is that cells can remember which genes are on or off. A second type of modification, called histone modification, affects DNA indirectly. DNA in cells is wrapped around histone proteins, which form spool-like structures that enable DNA’s very long molecules to be wound neatly into chromosomes inside the cell nucleus. Proteins...in turn... can attach a variety of chemical tags to histones.

As a human being has trillions of cells, specialized for different functions in muscles, bones and the brain, each cell still carries essentially the same genome in its nucleus. The epigenomic modifications allow differences to occur among cells and their function. For example, specialized cells in the eye turn on genes that make proteins that can detect light. Specialized cells in red blood cells make proteins that carry oxygen from the air to the rest of the body. The epigenome controls many of these changes to the genome or DNA.

Lifestyle and environmental factors such as smoking, diet and infectious disease can expose a person to pressures that prompt chemical responses. These responses lead to changes in the epigenome, some of which can be damaging and reduce longevity. For example, research has shown that chronic exposure to a stress hormone causes modifications to DNA prompting changes in gene expression.

These changes, like many others, impact the rate of ticking of the biological or age clock. What has been learned is that computed biological age based on DNA methylation extent closely predicts the chronological age of numerous tissues and cells to within just a few years. Certain tissues such as skeletal muscle, heart tissue and breast tissue however do not fit the computed biological age model (based on methylation extent) and do not allow accurate indication of age. Tissue changes impact the rate at which the biological or aging clock is ticking as shown by rates of change in DNA methylation. This biological or aging clock changes faster from birth to adulthood but then slows to a constant rate starting around the age of 20 years.

What does this teach us about longevity? The first twenty years of life exposures and the extent of epigenome modification of the genome clearly impacts longevity and the age to which we live. Our longevity might be summarized by the thought: If we only knew then... what we know now... about how to live our early years.

**Volume 2 Issue 5 December 2016**

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